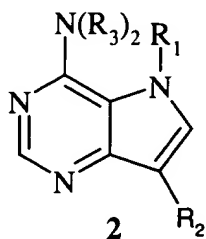


Applicants submit the instant amendment as a replacement for the amendment filed by Applicants on May 28, 2002.

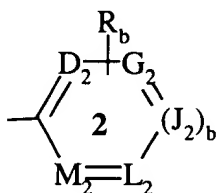
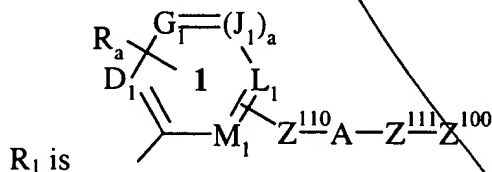
Please amend the above-identified application as follows:

In the Claims:

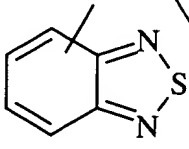
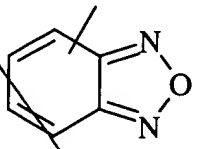
1. (Amended) A compound of Formula (I), the racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof,



wherein:



where Z<sup>100</sup> is or a group optionally substituted with R<sub>b</sub> selected from the group consisting of cycloalkyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,

thienyl, benzoxazolyl, benzothiazolyl, , , thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, benzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z<sup>110</sup> is a covalent bond, or an optionally substituted (C<sub>1</sub>-C<sub>6</sub>) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN,

OH, halogen, NO<sub>2</sub>, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z<sup>111</sup> is a covalent bond, an optionally substituted (C<sub>1</sub>-C<sub>6</sub>) or an optionally substituted -(CH<sub>2</sub>)<sub>n</sub>-cycloalkyl-(CH<sub>2</sub>)<sub>n</sub>-; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO<sub>2</sub>, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

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R<sub>a</sub> and R<sub>1</sub> each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, -NO<sub>2</sub>, -C(O)OH, -C(O)H, -OH, -C(O)O-alkyl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, -Z<sup>105</sup>-C(O)N(R)<sub>2</sub>, -Z<sup>105</sup>-N(R)-C(O)-Z<sup>200</sup>, -Z<sup>105</sup>-N(R)-S(O)<sub>2</sub>-Z<sup>200</sup>, -Z<sup>105</sup>-N(R)-C(O)-N(R)-Z<sup>200</sup>, R<sub>c</sub> and CH<sub>2</sub>OR<sub>c</sub>;

where R<sub>c</sub> for each occurrence is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, -CH<sub>2</sub>-NR<sub>d</sub>R<sub>e</sub>, -W-(CH<sub>2</sub>)<sub>t</sub>-NR<sub>d</sub>R<sub>e</sub>, -W-(CH<sub>2</sub>)<sub>t</sub>-Oalkyl, -W-(CH<sub>2</sub>)<sub>t</sub>-S-alkyl, or -W-(CH<sub>2</sub>)<sub>t</sub>-OH;

Z<sup>105</sup> for each occurrence is independently a covalent bond or (C<sub>1</sub>-C<sub>6</sub>);

Z<sup>200</sup> for each occurrence is independently a substituted or unsubstituted (C<sub>1</sub>-C<sub>6</sub>), substituted or unsubstituted phenyl or substituted or unsubstituted -(C<sub>1</sub>-C<sub>6</sub>)-phenyl;

R<sub>d</sub> and R<sub>e</sub> for each occurrence are independently H, alkyl, alkanoyl or SO<sub>2</sub>-alkyl; or R<sub>d</sub>, R<sub>e</sub> and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring; t for each occurrence is independently an integer from 2 to 6; W for each occurrence is independently a direct bond or O, S, S(O), S(O)<sub>2</sub>, or NR<sub>f</sub>, wherein R<sub>f</sub> for each occurrence is independently H or alkyl;

or R<sub>1</sub> is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with

ring 2;

R<sub>3</sub> is hydrogen, hydroxy, substituted or unsubstituted alkyl or substituted or unsubstituted alkoxy;

A is -O-; -S-; -S(O)<sub>p</sub>-; -N(R)-; -N(C(O)OR)-; -N(C(O)R)-; -N(SO<sub>2</sub>R)-; -CH<sub>2</sub>O-; -CH<sub>2</sub>S-; -CH<sub>2</sub>N(R)-; -CH(NR)-; -CH<sub>2</sub>N(C(O)R)-; -CH<sub>2</sub>N(C(O)OR)-; -CH<sub>2</sub>N(SO<sub>2</sub>R)-; -CH(NHR)-; -CH(NHC(O)R)-; -CH(NHSO<sub>2</sub>R)-; -CH(NHC(O)OR)-; -CH(OC(O)R)-; -CH(OC(O)NHR)-; -CH=CH-; -C(=NOR)-; -C(O)-; -CH(OR)-; -C(O)N(R)-; -N(R)C(O)-; -N(R)S(O)<sub>p</sub>-; -OC(O)N(R)-; -N(R)-C(O)-(CH<sub>2</sub>)<sub>n</sub>-N(R)-; -N(R)C(O)O-; -N(R)-(CH<sub>2</sub>)<sub>n+1</sub>-C(O)-; -S(O)<sub>p</sub>N(R)-; -O-(CR<sub>2</sub>)<sub>n+1</sub>-C(O)-; -O-(CR<sub>2</sub>)<sub>n+1</sub>-O-; -N(C(O)R)S(O)<sub>p</sub>-; -N(R)S(O)<sub>p</sub>N(R)-; -N(R)-C(O)-(CH<sub>2</sub>)<sub>n</sub>-O-; -C(O)N(R)C(O)-; -S(O)<sub>p</sub>N(R)C(O)-; -OS(O)<sub>p</sub>N(R)-; -N(R)S(O)<sub>p</sub>O-; -N(R)S(O)<sub>p</sub>C(O)-; -SO<sub>p</sub>N(C(O)R)-; -N(R)SO<sub>p</sub>N(R)-; -C(O)O-; -N(R)P(OR<sub>g</sub>)O-; -N(R)P(OR<sub>g</sub>)-; -N(R)P(O)(OR<sub>g</sub>)O-; -N(R)P(O)(OR<sub>g</sub>)-; -N(C(O)R)P(OR<sub>g</sub>)O-; -N(C(O)R)P(OR<sub>g</sub>)-; -N(C(O)R)P(O)(OR<sub>g</sub>)O-, or -N(C(O)R)P(OR<sub>g</sub>)-;

where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R<sub>g</sub> for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2;

or in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R and R<sub>g</sub> together form a five- or six-membered heterocyclic ring; or

A is NRSO<sub>2</sub> and R, R<sub>a</sub> and the nitrogen atom together form a substituted or unsubstituted five or six-membered heterocyclic ring fused to ring 1;

R<sub>2</sub> is -Z<sup>101</sup>-Z<sup>102</sup>;

$Z^{101}$  is a covalent bond,  $-(C_1-C_6)-$ ,  $-(C_1-C_6)-O-$ ,  $-(C_1-C_6)-C(O)-$ ,  $-(C_1-C_6)-C(O)O-$ ,  $-(C_1-C_6)-C(O)-NH-$ ,  $-(C_1-C_6)-C(O)-N((C_1-C_6))-$  or a substituted or unsubstituted phenyl group;

$Z^{102}$  is hydrogen, a substituted or unsubstituted alkyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted, saturated or unsaturated heterocyclic group, or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group;

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said substituted heterocyclic or substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, substituted or unsubstituted alkoxy, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido; substituted or unsubstituted amino, oxo, a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more nitrogen atoms, one or more oxygen atoms or a combination thereof;

wherein said nitrogen atoms are independently optionally substituted by a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; or

$R_2$  is of the formula B-E, wherein B is a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalkylcarbonyl, hydroxy, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylencarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted azacycloalkyl, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino or substituted or unsubstituted aryl;

a is 1 and  $D_1$ ,  $G_1$ ,  $J_1$ ,  $L_1$  and  $M_1$  are each independently selected from the group

consisting of  $CR_a$  and  $N$ , provided that at least two of  $D_1$ ,  $G_1$ ,  $J_1$ ,  $L_1$  and  $M_1$  are  $CR_a$ ; or

a is 0, and one of  $D_1$ ,  $G_1$ ,  $L_1$  and  $M_1$  is  $NR_a$ , one of  $D_1$ ,  $G_1$ ,  $L_1$  and  $M_1$  is  $CR_a$  and the remainder are independently selected from the group consisting of  $CR_a$  and  $N$ , wherein  $R_a$  is as defined above;

b is 1 and  $D_2$ ,  $G_2$ ,  $J_2$ ,  $L_2$  and  $M_2$  are each independently selected from the group consisting of  $CR_a$  and  $N$ , provided that at least two of  $D_2$ ,  $G_2$ ,  $J_2$ ,  $L_2$  and  $M_2$  are  $CR_a$ ; or

b is 0, and one of  $D_2$ ,  $G_2$ ,  $L_2$  and  $M_2$  is  $NR_a$ , one of  $D_2$ ,  $G_2$ ,  $L_2$  and  $M_2$  is  $CR_a$  and the remainder are independently selected from the group consisting of  $CR_a$  and  $N$ , wherein  $R_a$  is as defined above; and

n for each occurrence is independently an integer from 0 to 6.